NIBSC
Assuring the quality of biological medicines

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the collaborative study participants and Standard Processing Divsion for the filling

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.ac.uk
WHO Biological Standards: Http://www.who.int/biologicals/en/
JCTLM Higher order reference materials: http://www.bipm.org/jctlm
Derivation of International Units:
Http://www.nibsc.ac.uk/products/faq.asp
Ordering standards from NIBSC:
Http://www.nibsc.ac.uk/products/faq.asp
NIBSC Terms & Conditions: Http://www.nibsc.ac.uk/terms.html

12. CUSTOMER FEEDBACK

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to enquiries@nibsc.ac.uk

13. CITATION

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

14. MATERIAL SAFETY SHEET

Physical and Chemical properties		
Physical appearance: Freeze dried powder	Corrosive:	No
Stable: Yes	Oxidising:	No
Hygroscopic: No	Irritant:	No
Flammable: No	Handling:	See caution, Section 2
Other (specify):	Contains material of biological origin	
Toxicological properties		
Effects of inhalation:	Not established, avoid inhalation	
Effects of ingestion:	Not established, avoid ingestion	
Effects of skin absorption:	Not established, avoid contact with skin	
Suggested First Aid		
Inhalation:	Seek medical advice	
Ingestion: Seek medical advice		
Contact with eyes:	Wash with copious amounts of water. Seek medical advice	
Contact with skin:	Wash thoroughly with water.	
Action on Spillage and Method of Disposal		
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological waste.		

15. LIABILITY AND LOSS

Information provided by the Institute is given after the exercise of all reasonable care and skill in its compilation, preparation and issue, but it is provided without liability to the Recipient in its application and use.

It is the responsibility of the Recipient to determine the appropriateness of the standards or reference materials supplied by the Institute to the Recipient ("the Goods") for the proposed application and ensure that it has the necessary technical skills to determine that they are appropriate. Results obtained from the Goods are likely to be dependant on conditions of use by the Recipient and the variability of materials beyond the control of the Institute.

All warranties are excluded to the fullest extent permitted by law, including without limitation that the Goods are free from infectious agents or that the supply of Goods will not infringe any rights of any third party.

The Institute shall not be liable to the Recipient for any economic loss whether direct or indirect, which arise in connection with this agreement.

The total liability of the Institute in connection with this agreement, whether for negligence or breach of contract or otherwise, shall in no event exceed 120% of any price paid or payable by the Recipient for the supply of the Goods.

If any of the Goods supplied by the Institute should prove not to meet their specification when stored and used correctly (and provided that the Recipient has returned the Goods to the Institute together with written notification of such alleged defect within seven days of the time when the Recipient discovers or ought to have discovered the defect), the Institute shall either replace the Goods or, at its sole option, refund the handling charge provided that performance of either one of the above options shall constitute an entire discharge of the Institute's liability under this Condition.

16. INFORMATION FOR CUSTOMS USE ONLY

Country of origin for customs purposes*: United Kingdom * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
Net weight: 1 - 2g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable. **Attached:** No

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WHO International Standard
Acellular Pertussis Vaccine 1st IS
NIBSC code: JNIH-3
Instructions for use
(Version 6.0, Dated 22/01/2009)

1. INTENDED USE

JNIH-3 is a freeze-dried two components (PT, FHA) acellular pertussis vaccine manufactured by the Biken Kanonji Institute, Japan. The freeze-dried ampoules were originally held by the Statens Serum Institut (SSI), Copenhagen, Denmark and subsequently transferred to NIBSC.On behalf of WHO and in collaboration with members from NIID, Japan, NICPBP, China and KFDA, South Korea, a collaborative study for the establishment of JNIH-3 as a common standard for acellular pertussis vaccine in the modified intra-cerebral challenge assay (MICA, modified Kendrick test) was organized by NIBSC in 2006. Fourteen laboratories performed MICA in the study. The results of this study show that using JNIH-3 as a standard would improve inter-laboratory agreement in potency estimates for acellular pertussis vaccine formulations. This study did not show significant dissimilarity between JNIH-3 and the various acellular pertussis vaccine formulations included, irrespective of the differences in acellular pertussis components. Available data indicates that JNIH-3 is sufficiently stable to serve as an international standard. In 2008, on the basis of the results of this study (WHO/BS/08.2086), preparation JNIH-3 has been established as the First International Standard for Acellular Pertussis Vaccine for use in the MICA and other protective bioassays.

2. CAUTION

This preparation is not for administration to humans.

The material is not of human or bovine origin. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

34 IU per ampoule.

4. CONTENTS

Country of origin of biological material: Japan.
Each ampoule of JNIH-3 (Japanese National Institute of Health) contains one ml of a co-purified two component acellular pertussis vaccine absorbed onto aluminium phosphate, manufactured by the Biken Kanonji Institute in Japan in 1984 . At the time of preparation each ampoule was found to contain a mean of 27.25 mg dry materials :

Protein nitrogen	15.0 µg PN
Filamentous Haemagglutinin (FHA)	7.5 µg PN
Pertussis Toxin (PT)	7.7 µg PN
Haemacell	20 mg
Aluminium	0.2 mg
Formaldehyde	<15 µg
Thiomersal	0.1 mg

5. STORAGE

Unopened ampoules should be stored at -20°C.

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body.
Tap the ampoule gently to collect the material at the bottom (labeled) end. Ensure that the disposable ampoule safety breaker provided is pushed down on the stem of the ampoule and against the shoulder of the ampoule body. Hold the body of the ampoule in one hand and the disposable ampoule breaker covering the ampoule stem between the thumb and first finger of the other hand. Apply a bending force to open the ampoule at the coloured stress point, primarily using the hand holding the plastic collar.
Care should be taken to avoid cuts and projectile glass fragments that might enter the eyes, for example, by the use of suitable gloves and an eye shield. Take care that no material is lost from the ampoule and no glass falls into the ampoule. Within the ampoule is dry nitrogen gas at slightly less than atmospheric pressure. A new disposable ampoule breaker is provided with each DIN ampoule.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze dried powder prior to reconstitution. Ampoules of JNIH-3 should be reconstituted in sterile saline and used according to laboratories own methodology. It is not recommended to store the reconstituted material under any conditions, if it is not used in the same day.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

1) Collaborative Study Report (2008) D. Xing, P. Newland, Y. Horiuchi, S. Zhang, Y. Kim, M. Corbel and R. Gaines-Das. International Collaborative Study on Reference Preparations Used for Modified Intra-Cerebral Challenge Assay for Acellular Pertussis Vaccines
WHO/BS/08.2086

2) D.K.L. Xing, M.J. Corbel, R. Dobbelaer and I. Knezevic. WHO Working Group on standardisation and control of acellular pertussis vaccines- report of a meeting held on 16-17 March 2006, St. Albans, United Kingdom, Vaccine 2007, 25:2749-2757

3) JG Kreeftenberg
Collaborative study on the candidate reference materials JNIH-3, JNIH-4, JNIH- 5 for the assay of acellular pertussis vaccines.
WHO BS/88.1586

10. ACKNOWLEDGEMENTS

Grateful acknowledgement is made to Dr Paul Matejtschuk (NIBSC) for moisture and oxygen determinations for JNIH-3. We also thank all of the participants of the collaborative study for their helpful contributions and the various manufacturers who contributed products for inclusion in this study via the national control authorities.

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Net weight: 0.5 - 1.0 g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable. **Attached:** No

Ⅲ. 研究成果の刊行に関する一覧表

別紙４

研究成果の刊行に関する一覧表レイアウト

書籍
該当無し

雑誌　以下の論文別刷りは総合研究報告書に３ヶ年分をまとめて掲載した

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Mizukami T, Masumi A, Momose H, Kuramitsu M, Takizawa K, Naito S, Maeyama J-I, Furuhata K, Tsuruhara M, Hamaguchi I, Yamaguchi K	An improved abnormal toxicity test by using reference vaccine-specific body weight curves and histopathological data for monitoring vaccine quality and safety in Japan	Biologicals	37	8-17	2009
Hamaguchi I, Imai J-I, Momose H, Kawamura M, Mizukami T, Naito S, Maeyama J-I, Masumi A, Kuramitsu M, Takizawa K, Kato H, Mizutani T, Horiuchi Y, Nomura N, Watanabe S, Yamaguchi K	Application of quantitative gene expression analysis for pertussis vaccine safety control	Vaccine	26	4689-4696	2008
Mizukami T, Imai J-I, Hamaguchi I, Kawamura M, Momose H, Naito S, Maeyama J-I, Masumi A, Kuramitsu M, Takizawa K, Nomura N, Watanabe S, Yamaguchi K	Application of complementary DNA microarray technology to influenza A/Vietnam/1194/2004 (H5N1) vaccine safety evaluation	Vaccine	26	2270-2283	2008

その他
「ワクチン等の国家検定に係わる国際動向と我が国の現状と課題」記録集
国立感染症研究所セミナー　平成20年12月2日

Ⅳ. 研究成果の刊行物・別刷

総合研究報告書にまとめて掲載した